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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/757,673	01/10/2001	James M. Wilson	GNVPN.019BIUSA	8771

270 7590 07/30/2002

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EXAMINER

SHUKLA, RAM R

ART UNIT PAPER NUMBER

1632

DATE MAILED: 07/30/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/757,673

Applicant(s)

WILSON ET AL.

Examiner

Ram Shukla

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 May 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 7-24 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 7-10 and 12-24 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 9.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: *detailed action*.

DETAILED ACTION

1. Amendment and response filed 5-14-02 has been received.
2. Claim 11 has been cancelled.
3. Amendments to claims 7-10, 12 and 13 have been entered.
4. New claims 18-24 have been entered.
5. Claims 7-10 and 12-24 are pending and under consideration in the instant application.
6. The abstract has been entered.

Claim Objections

7. New claim 18, 23 and 24 are objected because they do not consistently use one abbreviation for one term, a recombinant adeno-associated virus or rAAV. Consistent use of one term is suggested for clarity.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 7-10 and 12-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Amended claims 7, 12 and 13 and new claims 18, 23 and 24 recite the embodiment "wherein the recombinant AAV is at least as free of the contaminating adenoviral helper virus as is obtained by subjecting said recombinant AAV to four rounds of cesium chloride gradient centrifugation" which would encompass "equal to" or "more" pure recombinant AAV composition compared to the preparation of recombinant AAV obtained after four rounds of cesium chloride centrifugation.

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However, the specification does not provide written support either for the phrase it self or for equal to or more pure AAV preparation compared to that obtained by four rounds of cesium chloride centrifugation. It is noted that Applicants did not provide any guidance as to where in the specification the explicit or implicit support for the phrase was provided. It is reiterated that the specification only discloses that the composition was subjected to four rounds of cesium chloride gradient centrifugation and there is no written support in the specification as what would be the contaminating levels of adenoviral helper virus after four rounds of cesium chloride centrifugation and therefore, an artisan would not know what contamination level would be considered to be "at least as free of the contaminating adenoviral helper virus". When an amendment is filed in reply to an objection or rejection based on 35 U.S.C.112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure. See MPEP 2163.06

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 7-10 and 12-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 7, 12, 13, and newly presented claims 18, 23 and 24 are vague and indefinite because the metes and bounds of the claimed invention is not clearly defined as set forth in the previous office action of 11-23-01. It is noted that the amendment to claims 7, 12, and 13 have used a different phrase, however, the specification does not disclose what would be considered the contaminating levels of adenoviral helper virus in the recited recombinant AAV composition that is purified by four rounds of cesium chloride gradient centrifugation. Therefore the metes and bounds of the claimed invention is not clear. It is noted that except for

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a statement that the amendment renders the rejection moot, applicants did not provide any evidence as to how the rejection is rendered moot.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 7-10 and 12-24 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 5,866,552 (Wilson JM et al., 2-2-1999) for reasons of record set forth in the previous office action of 11-23-01.

Applicants' request that this rejection be deferred until allowance is acknowledged.

13. Claims 7-10 and 12-24 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6, 9, 20, 21, 23, 25, 26, and 27 of co-pending Application No. 09/237,064 for reasons of record set forth in the previous office action of 11-23-01.

Applicants' request that this rejection be deferred until allowance is acknowledged.

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14. Claims 7-10 and 12-24 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 18-24 and 26-28 and 30-35 of co-pending Application No. 09/242,977 for reasons of record set forth in the previous office action of 11-23-02 for reasons of record set forth in the previous office action of 11-23-01.

Applicants' request that this rejection be deferred until allowance is acknowledged.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. Claims 7-10, 18 and 23 are rejected under 35 U.S.C. 102(e) as being anticipated by Podsakoff et al (US 5,858,351, 1-12-1999, filing date 1-18-1996, ref. # AI in the IDS filed 3-16-01) for reasons of record set forth in the previous office action of 11-23-01.

Response to Arguments

Applicant's arguments filed 5-7-02 have been fully considered but they are not persuasive. Applicants' arguments that the Examiner has admitted under 103 that Podsakoff does not teach AAV comprising ApoE is incorrect and irrelevant because claims 7-10 are not directed to AAV comprising ApoE. In contrast to applicants arguments, Podsakoff references teaches to inject the rAAV vector in mice intramuscularly in heart and cardiac muscles (see col 19 continued in col 20) and that erythropoietin is secreted by the myotubes or myoblasts. Podsakoff reference further teaches that EPO gene was used as an example and that other

suitable DNA sequences could be used that encode for proteins used for the treatment of different diseases (see lines 31-67 in column 10).

Therefore, the invention of claims 7-10, 18 and 23 is anticipated by Podsakoff et al and the rejection is maintained.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

9. Claims 7-10 and 18-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Podsakoff et al (US 5,858,351, 1-12-1999, filing date 1-18-1996, ref. # AI in the IDS filed 3-16-01) in view of Kashyap et al. (Journal of Clinical Investigation 96:1612-1620, ref# CU in the IDS filed 3-16-01) for reasons of record set forth in the previous office action of 11-23-01.

Regarding the newly presented claims 18-24 it is noted that the limitations of claims 18 and 23 are encompassed by claims 7-10. Accordingly, the discussion in the office action of 11-23-01 are applicable here. Regarding claims 19-22, it is noted that the limitations recited are conventional in the art and an artisan would have standardized the number of particles in the composition or monitored the expression levels of a transgene after delivering the vector to a mammal.

Response to Arguments

Applicant's arguments filed 5-7-02 have been fully considered but they are not persuasive. Applicants' arguments that the defects of Podsakoff reference are not overcome by Kashyap reference are not persuasive because the teaching of Kashyap considered in the instant case is the DNA encoding ApoE and other

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limitations are taught by Podsakoff. As noted in the previous office action, an artisan would have used AAV in view of the teachings of Podsakoff that adenoviral vector gene expression is decreased due to immune reaction. It is noted that the applicants have not provided any evidence to support their arguments.

Therefore, the rejection of claims 7-10 and 18-24 is maintained.

10. Claims 7-10 and 12-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Podsakoff et al 1999 in view of Fang et al 1995 (Fang B et al Human Gene Therapy 6:1039-1044, 1995, ref. # CS in the IDS filed 3-126-01) and Kay et al (US 5,980, 886, 11-9-1999) for reasons of record set forth in the previous office action of 11-23-01.

Response to Arguments

Applicant's arguments filed 5-7-02 have been fully considered but they are not persuasive. Applicants' arguments that Fang, Kay do not teach intramuscular delivery is not persuasive since Podsakoff et al teaches intramuscular delivery of a transgene. Therefore, there is no question of deficiency of this aspect in Podsakoff. As far as factor IX delivery is concerned, Podsakoff et al also teaches that its vector and method can be used for treatment of several diseases such as anemias, thalassemia and hemophilia (see lines 31-42 in col 10) and an artisan would have been motivated to use an adeno-associated viral vector in place of adenoviral vector in view of the teachings of Fang et al that adenoviral vector mediated gene delivery results only in transient gene expression due to immune response.

11.No claim is allowed.

When amending claims, applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c). For instructions, Applicants are referred to

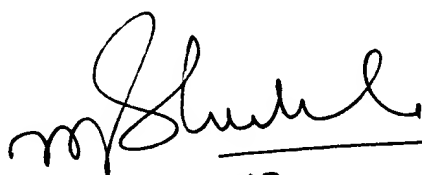
<http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm>.

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Applicants are also requested to submit a copy of all the pending/under consideration claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Dianiece Jacobs whose telephone number is (703) 305-3388.

Ram R. Shukla, Ph.D.


RAM R. SHUKLA, PH.D
PATENT EXAMINER